Package ‘spef’

October 14, 2022

Title  Semiparametric Estimating Functions
Version  1.0.9
Depends  R (>= 3.4.0)
License  GPL (>= 3)
URL  http://github.com/stc04003/spef
BugReports  http://github.com/stc04003/spef/issues
Encoding  UTF-8
LazyData  true
RoxygenNote  6.1.1
Imports  BB, SQUAREM, ggplot2, methods, sm, survival, plyr, nleqslv
NeedsCompilation  yes
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Repository  CRAN
Date/Publication  2020-05-24 05:00:02 UTC

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Description

spef is an R package that consists of a collection of functions for fitting semiparametric regression models for panel count survival data. Estimating procedures include: Wang-Yan’s augmented estimating equations (AEE, AEEX), Huang-Wang-Zhang’s method (HWZ), Zhang’s maximum pseudolikelihood (MPL), Maximum pseudolikelihood with I-Splines (MPLs), Maximum likelihood with I-Splines (MLs), Sun-Wei’s method (‘EE.SWa’, ‘EE.SWb’, ‘EE.SWc’), Hu-Sun-Wei’s method (‘EE.HSWc’, ‘EE.HSWm’), and accelerated mean model (‘AMM’).

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References


See Also

Useful links:

- [http://github.com/stc04003/spef](http://github.com/stc04003/spef)

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**bladTumor**  
**Bladder Tumors Cancer Recurrences**

Description

A data frame contains data on recurrences of bladder cancer, used by many people to demonstrate methodology for recurrent event modeling. The data was obtained by courtesy of Ying Zhang, containing records of 118 patients from three treatment arms: 48 are from the placebo arm, 37 are from the thiotepa arm, and the rest 33 are from the pyridoxine arm.

Usage

```r
data(bladTumor)
```

Format

A data frame contains the following columns:

- **subject**: patient id
- **time**: observation time
- **count**: cumulative number of tumors
- **count2**: number of new tumors since last observation time
- **number**: initial number of tumors (8=8 or more)
- **size**: size (cm) of largest initial tumor
- **pyridoxine**: dummy variable for pyridoxine arm
- **thiotepa**: dummy variable for thiotepa arm

Note

To our surprise, the two-treatment (placebo and thiotepa) subset of the full version bladTumor do not match the two-treatment version blaTum.
References


See Also

blaTum

Examples

```r
data(blaTum)
## Plot bladder tumor data
p <- plot(with(blaTum, PanelSurv(subject, time, count2)))
print(p)
```

blaTum | Bladder Tumors Cancer Recurrences

Description

A data frame contains data on recurrences of bladder cancer, used by many people to demonstrate methodology for recurrent event modelling. This data set organized differently from bladTumor. The data contains records of 85 patients from two treatment arms: 48 are from the placebo arm, and the rest 37 are from the thiotepa arm.

Usage

data(blaTum)

Format

A data.frame contains the following columns:

- **id**: patient id
- **treatment**: placebo = 0, thiotepa = 1
- **size**: size (cm) of largest initial tumor
- **num**: initial number of tumors (8 = 8 or more)
- **time**: observation time
- **count**: number of new tumors since last observation time
Note

To our surprise, the two-treatment (placebo and thiotepa) subset of the full version bladTumor do not match the two-treatment version bladTum.

References


See Also

bladTumor

Examples

data(blaTum)
library(ggplot2)
ggplot(blaTum, aes(time, id)) + geom_tile(aes(fill=count)) +
   facet_grid(treatment ~ ., scales="free_y", )

---

panelReg

Fits Semiparametric Regression Models for Panel Count Survival Data

Description

Fits an proportional means model:

\[
\Lambda(t; X_i) = E[N_i(t)|X_i] = \Lambda(t)e^{X_i \beta},
\]

where \( \beta \) is a \( p \times 1 \) vector of covariate coefficient and \( \Lambda(\cdot) \) is a completely unspecified baseline mean function.

Estimating procedures include: Wang-Yan’s augmented estimating equations ("AEE", "AEEX"), Huang-Wang-Zhang’s method ("HWZ"), Zhang’s maximum pseudo-likelihood ("MPL"), Maximum pseudolikelihood with I-Splines ("MPLs"), Maximum likelihood with I-Splines ("MLs"), Sun-Wei’s method ("EE.SWa", "EE.SWb", "EE.SWc"), and Hu-Sun-Wei’s method ("EE.HSWc", "EE.HSWm").

The function can also fits an accelerated mean model ("AMM"):

\[
\Lambda(t; X_i) = E[N_i(t)|X_i] = \Lambda(te^{X_i \beta})e^{X_i \beta}.
\]
Usage

panelReg(formula, data, method = c("AEE", "AEEX", "HWZ", "MPL", "MPLs", "MLs", "AMM", "EE.SWa", "EE.SWb", "EE.SWc", "EE.HSWc", "EE.HSWm"), se = c("NULL", "smBootstrap", "Bootstrap", "Impute", "Sandwich"), control = list())

Arguments

- formula: A formula object, with the response on the left of a "~" operator, and the terms on the right. The response must be a panel count survival object as returned by function PanelSurv.
- data: A data.frame in which to interpret the variables named in the formula. Three variables including subjects' id, observation times, and number of new events since last observation time are required to feed into function PanelSurv as response. At least one covariate variable is required.
- method: Fitting method. See 'Details'.
- se: Standard error estimation method. See 'Details'.
- control: A list of control parameters. See 'Details'.

Details

Some assumptions details about the observation times and censoring time need clarification. Three possible scenarios of observation times are considered: 1) independent observation times – the observation times are independent of the underlying recurrent event process; 2) conditional independent observation times – the observation times are independent of the event process given observed covariates; 3) informative observation times – after conditioning on observed covariates, the observation times and the event process are still dependent through an unobserved multiplicative frailty. Similarly, the three scenarios apply to the censoring time.

"AEE" and "AEEX" are the augmented estimating equation methods under conditional independent censoring and informative censoring respectively. Both allow informative observation times.

"HWZ" is Huang-Wang-Zhang’s method. It allows both information observation times and informative censoring time. It does not need to specify the dependence structure or model the frailty.

"MPL" and "MPLs" are maximum pseudolikelihood methods, with nonparametric and monotone spline estimates of the baseline mean function respectively. They assume conditional independent observation times and censoring time. The underlying event process is assumed to be Poisson, and the within subjects dependence is ignored.

"MLs" is maximum likelihood method with monotone splines estimates of the baseline mean function. It assumes conditional independent observation times and censoring time, and a Poisson underlying event process.

"EE.SWa", "EE.SWb" and "EE.SWc" are estimating equation approaches based on Sun-Wei's methods. The first assumes independent observation times and censoring time. The second assumes conditional independent observation times but independent censoring time. The third assumes conditional independent observation times and censoring time. All three variations work on centered covariates and avoid estimating the baseline mean.
"EE.HSWc" and "EE.HSWm" are estimating equation approaches based on Hu-Sun-Wei’s methods. The first assumes independent observation times and censoring time. The second assumes conditional independent observation times but independent censoring time. Both variations work on centered covariates and avoid estimating the baseline mean.

"AMM" is the accelerated mean model. The observation time process is allowed to be correlated with the underlying recurrent event process through a frailty variable, which does not need to be specified. The model also allows marginal interpretations for the regression parameters and connects naturally with AFT model. See Chiou et al. (2017) for more details.

For standard errors estimation method:
"NULL" means do not calculate standard errors; "smBootstrap" is the smoothed bootstrap estimation method that works with "AMM". "Bootstrap" works with all fitting methods; "Impute" is the multiple imputation method that works with "AAE" and "AEEX"; "Sandwich" is the robust sandwich estimation method that works with "AAE" and "AEEX".

The control argument is a list that can supply any of the following components:

- betaInit: Object of class "numeric", initial value for covariate coefficient, default 0.
- interval: Object of class "numeric", initial search interval for solving beta, default (-5, 5).
- maxIter: Object of class "numeric", maximum iteration allowed, default 500 for "AEEX" and "HWZ", 150 for others.
- absTol: Object of class "numeric", absolute tolerance, default 1e-6.
- relTol: Object of class "numeric", relative tolerance, default 1e-6.
- a: Object of class "numeric", a tune parameter, default 0.1. In the case of gamma frailty, "a" corresponds to the value of both shape and rate parameters.
- R: Object of class "numeric", number of bootstrap or imputation, default 30.

Value
An object of S3 class "panelReg" representing the fit. See panelReg.object for details.

References

See Also

panelReg.object

Examples

```r
## Not run:
data(blaTum)
## Fit the bladder tumor data set
formula <- PanelSurv(id, time, count) ~ num + size + treatment

panelReg(formula, data = blaTum, method = "AEE", se = "Sandwich")
panelReg(formula, data = blaTum, method = "AEEX", se = "Impute",
        control = list(a = 0.1, R = 30))
panelReg(formula, data = blaTum, method = "HWZ", se = "Bootstrap",
        control = list(R = 30))
panelReg(formula, data = blaTum, method = "MLs", se = "NULL")
panelReg(formula, data = blaTum, method = "EE.SWa", se = "Bootstrap",
        control = list(R = 30))
panelReg(formula, data = blaTum, method = "EE.HSWc", se = "Bootstrap",
        control = list(R = 30))

## End(Not run)
```

panelReg.object  
*Semiparametric Panel Count Regression Object*

Description

This S3 class of objects is returned by the `panelReg` class of functions to represent a fitted semiparametric panel count regression model. Objects of this class have methods for the functions `print` and `plot`.

Value

- **beta** a vector, estimated coefficients of the linear predictor.
- **baseline** a step function or spline function, estimated cumulative baseline mean.
- **timeGrid** a vector, ordered unique set of observation times.
- **lambda** a vector, estimated baseline mean for each interval.
- **convergence** an integer code, 0 indicates successful convergence, error code 1 indicates that the iteration limit `maxIter` had been reached.
iter an integer value, number of interactions when stopped.

betaSE a vector, estimated standard errors of beta.

betaVar a matrix, estimated covariance matrix of beta.

baselineSE a vector, estimated standard error of cumulative baseline mean.

See Also

panelReg

PanelSurv

Create a PanelSurv Object

Description

Create a panel count survival object, usually used as a response variable in a model formula.

Usage

PanelSurv(ID, time, count)

is.PanelSurv(x)

Arguments

ID Observation subject's ID.

time Observation time.

count Observation subject's ID.

x An PanelSurv object.

Value

An object of S3 class "PanelSurv".

psDF a data frame, part of original input data frame with variable "ID", "time" and "count".

timeGrid ordered distinct observation times in the set of all observation times.

panelMatrix a matrix representation of panel count data, one row per subject, one column per time point in "timeGrid".

In the case of is.PanelSurv, a logical value TRUE if x inherits from class "PanelSurv", otherwise FALSE.

In the case of plot.PanelSurv, a tile plot of panelMatrix produced by package ggplot2 with color indicating number of counts since last observation time.

See Also

panelReg
Examples

```r
data(blaTum)
response <- with(blaTum, PanelSurv(id, time, count))
is.PanelSurv(response)
plot(response)
```

---

**plot.panelReg**

Plot a panelReg Object.

### Description

Plot the estimated baseline mean function. If "se" option of panelReg is not "NULL", 95 interval is also plotted.

### Usage

```r
## S3 method for class 'panelReg'
plot(x, ...)
```

### Arguments

- `x`  The result of a call to the panelReg function.
- `...`  Other graphical parameters such as line type, color, or axis labels.

### See Also

- `panelReg`
- `panelReg.object`

### Examples

```r
data(blaTum)
## Plot the fit of bladder tumor data set
fm <- PanelSurv(id, time, count) ~ num + size + treatment
fit1 <- panelReg(fm, data=blaTum, method = "AEE", se = "Sandwich")
plot(fit1)

fit2 <- panelReg(fm, data=blaTum, method = "MLs", se = "NULL")
plot(fit2)
```
plot.PanelSurv

**Description**

Plot the tile plot from a PanelSurv object.

**Usage**

```r
## S3 method for class 'PanelSurv'
plot(x, heat = FALSE, order = TRUE, ...)
```

**Arguments**

- `x`: an object of class `PanelSurv`.
- `heat`: an optional logical value indicating whether a swimmer-plot-like tile plot will be produced.
- `order`: an optional logical value indicating whether the tile plot will be sorted by the largest observation time.
- `...`: future extension

**Value**

A `ggplot` object

---

skinTumor

**Skin cancer chemoprevention trial**

**Description**

A data frame contains data on the recurrence of skin tumor. The original data is available in Table A.3. of Sun and Zhao (2013). This dataset contains records of 290 patients.

**Usage**

```r
data(skinTumor)
```
Format

This data frame contains the following columns:

id : patient id (repeated for each recurrence).
time : observation time.
age : patient’s age at enrollment.
male : gender; male = 1, female = 0.
dfmo : treatment (DFMO) group = 1; placebo = 0.
priorTumor : number of prior tumor from diagnosis to randomization.
countBC : number of newly developed basal cell carcinomas tumors since last observation time.
countSC : number of newly developed squamous cell carcinomas tumors since last observation time.
count : number of newly developed non-melanoma tumors since last observation time; this is equal to countBC + countSC.

References


See Also

skiTum

Examples

data(skinTumor)
library(ggplot2)
ggplot(skinTumor, aes(time, id, width = 25, height = 2)) +
  geom_tile(aes(fill = count)) + theme_bw() +
  facet_grid(dfmo ~ ., scales = “free_y”, as.table = FALSE,
            labeller = labeller(dfmo = function(x) paste(“DFMO =”, x))) +
  scale_fill_gradient(low = "grey", high = “black”) +
  scale_x_continuous(breaks = seq(0, 2000, 200)) +
  labs(fill = “Count”) + xlab(“Time in days”)
skiTum

A Simulated Data Mimicking a Skin Cancer Chemoprevention Trial

Description

A data frame contains data on the recurrence of skin tumor. This simulated data is created for illustrative purpose and it mimic the Skin Cancer Chemoprevention Trial used in Chiou et al. (2017). This data set contains records of 100 simulated patients.

Usage

data(skiTum)

Format

This data frame contains the following columns:

id : patient id (repeated for each recurrence).
time : observation time.
age : patient’s age at enrollment; age = 1 if greater than 65, age = 0 otherwise.
males : gender; male = 1, female = 0.
dfmo : treatment (DFMO) group = 1; placebo = 0.
priorTumor : number of prior tumor from diagnosis to randomization.
count : number of new tumors since last observation time.

See Also

skinTumor

Examples

data(skiTum)
library(ggplot2)
skitum$dfmo <- factor(skitum$dfmo, levels = c(1, 0), labels = c("placebo", "DFMO"))
ggplot(skitum, aes(time, id, height = 2, width = 25)) +
  geom_tile(aes(fill = count)) + theme_bw() +
  facet_grid(dfmo ~ ., scales = "free_y") +
  scale_fill_gradient(low = "grey", high = "black") + labs(fill="Count") +
  scale_x_continuous(breaks = seq(0, 1800, 100)) + xlab("Time in days")
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